REMARKS

The Amendment

The amendment to Claim 30 corrects a grammatical error in the claim.

No new matter is added in the amendments. The Examiner is respectfully requested to enter the amendments.

The Response

Objection to Specification

The disclosure is objected to by the Examiner because the first line of the specification allegedly needs to be updated to include priority information.

The specification is amended to include the updated priority information. Therefore, the objection to the disclosure should be withdrawn.

35 U.S.C. §112 First Paragraph Rejection

Rejection to Claims 36-37

Claims 36-37 are rejected under 35 U.S.C. § 112, first paragraph because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. Applicants respectfully traverse this rejection in light of the following comments.

The hybridoma which produces monoclonal antibody M195 was deposited with the American Type Culture Collection in Rockville, MD, USA 20852, under the ATCC Accession No. HB 10306 on December 14, 1989. The deposit was made pursuant to the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (Budapest Treaty). (*See* U.S. Patent No. 5,730,982, col. 5, lines 41-48).

Therefore, the rejection to Claims 36-37 should be withdrawn.

Rejection to Claims 30-45

Claims 30-45 are rejected under 35 U.S.C. § 112, first paragraph, because the

specification, while being enabling for a mutant antibody that comprises an amino acid substitution that eliminates a variable region framework glycosylation site, allegedly does not reasonably provide enablement for a mutant antibody that comprises an amino acid substitution that eliminates a variable region CDR glycosylation site. This rejection is respectfully traversed.

The pending claims are directed to mutant antibodies with increased affinity for an antigen through the elimination of a pre-existing glycosylation site in a variable region of an immunoglobulin. The variable region, as defined within the specification, consists "of a 'framework' region interrupted by three hypervariable regions, also called CDR's." Page 9, lines 8-10. Contrary to the Examiner's assertions, the specification teaches glycosylation through the entire variable region, not only within the framework region.

As the Examiner has acknowledged, the specification does teach alteration of glycosylation sites in the framework variable region. The specification teaches both N-glycosylation sites, which the Examiner acknowledges at position 73 in the M195 antibody, as well as other glycosylation sites, including O-linked glycosylation sites. See page 6, line 36 to page 7, line 30. The specification also teaches the type of glycosylation modification *within CDR's* in a "V region glycosylation site." See page 12, line 16 to page 13, line 7. The specification directs that glycosylation sites within CDR's are retained where "the parent immunoglobulin specifically binds an epitope that contains carbohydrate." However, the situation differs for epitopes with no glycosylation sites. In this case, the specification calls for such "glycosylation sites occurring in a CDR are preferably eliminated by mutation." Therefore, the specification teaches modification not only of the framework region within the variable region, but also in the CDR's of the variable region depending on the presence of glycosylation sites within the epitope.

Applicants respectfully submit that the Rudikoff reference (PNAS USA 79:1979 (1982)) cited by the Examiner does not support the Examiner's contentions in regards to glycosylation sites within the CDR. Rudikoff only teaches that an amino acid substitution at position 35 of a glutamic acid to alanine alters binding affinity. Rudikoff does not teach alteration of glycosylation sites within the CDR region through amino acid substitution, as the instant application does. *See* Rudikoff abstract. Moreover, Rudikoff does not teach that all amino acid changes within the CDR will result in binding affinity changes, only that amino acid mutations in

antibodies "may in *some* situations be effective in altering antigen-binding specificity." *See* Rudikoff abstract (emphasis in original). In contrast, the specification gives specific and explicit guidance as to what amino acids in a glycosylation recognition site should be altered.

As further support of the explicit and specific guidance that the instant invention provides, and that the instant invention does not require undue experimentation, the specification does not teach mutations within the entire variable region of the immunoglobulin. Rather, the mutations are limited to a small fraction of the amino acids within the variable region, only that where glycosylation sites are found. Therefore, in any immunoglobulin chain, identifying which sites to mutate does not involve undue experimentation. The specification provides more than adequate disclosure on how one of ordinary skill in the would enable the instant application.

Therefore, the specification discloses alteration of glycosylation sites throughout the variable region of immunoglobulin chains. Applicants respectfully request that the rejection be withdrawn.

Non-Statutory Obviousness-Type Double Patenting Rejection

Claims 30-45 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-16 of U.S. Patent No. 6,350,861. Applicants submit an executed terminal disclaimer herewith to overcome this rejection.

Therefore, the rejection should be withdrawn.

35 U.S.C. §102(a) Rejection

Claims 30-45 are rejected under 35 U.S.C. §102(a) as being anticipated by Co *et al.* (Journal of Immunology 148:1149-1154, February 15, 1992). The rejection is traversed because the cited article describes Applicants' own work.

Applicants' disclosure of his or her own work within a year before the application filing date cannot be used against him or her under 35 U.S.C. §102(a). (In re Katz, 607f.2d 450, 205 USPQ 14 CCTA 1992)). Applicants are submitting herewith a Declaration (See Exhibit A) pursuant to 37 CFR §1.132 to establish that the cited article is describing Applicants' own work.

The authorship of the cited article is different from the inventive entity of this application because there are additional authors, Drs. Nevenka M. Avdalovic, Philip C. Caron and Mark V.

Avdalovic, in the cited publication. According to the Declaration by Dr. Queen, enclosed herewith, the cited article describes Applicants' own work, such work was solely established in Dr. Queen's laboratory. Drs. Avdalovic and Caron contributed neither to concept formulation nor to research progress for the present invention. At the time of the publication, Drs. Avdalovic and Caron worked under the direction of Dr. Queen. There has been no evidence that Drs. Avdalovic and Caron have refused to disclaim inventorship or believes him or herself to be an inventor.

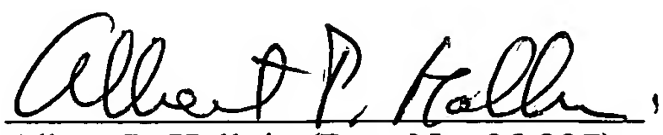
In view of the Declaration submitted, Applicants respectfully request the Examiner to withdraw the §102(a) rejection over Claims 30-45.

CONCLUSION

Applicants believe that the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 463-8109.

Respectfully submitted,

Date: February 23, 2004



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